Interplay of chronic kidney disease and intracerebral hemorrhage: Prognostic factors and clinical implications

By Chandrashekhar Enuguri

WORD COUNT	3027	TIME SUBMITTED	27-AUG-2025 11:24AM
		PAPER ID	117907013

Interplay of chronic kidney disease and intracerebral hemorrhage: Prognostic factors and clinical implications

Chandrashekhar Enuguri[1], Abhilash Tadiboina[2], Anish Mehta[1], Pooja Dugani[3], Pradeep Rangaiah[1], Mahendra Javali[1], Purushottam Acharya[1]

1Department of Neurology, Ramaiah Medical College and Hospitals, Ramaiah University of Applied Sciences, Bengaluru, India

2Trust in Hospitals, Bengaluru, India

3 Medanta - The Medicity, Gurgaon, India

Chandrashekhar Enuguri **ORCID ID:** 0009-0003-2743-0473

Anish Mehta **ORCID ID:** 0000-0003-0200-1835

Pooja Dugani **ORCID ID:** 0000-0003-2222-637X

Pradeep Rangaiah **ORCID ID:** 0000-0002-8427-3457

Mahendra Javali **ORCID ID:** 0000-0002-1094-7965

Purushottam Acharya **ORCID ID:** 0000-0002 -8225-5300

Corresponding author:

Anish Mehta

Email: anishmehta1302@gmail.com

ABSTRACT

Introduction. CKD significantly increases stroke risk, especially in ESKD patients, with a four- to ten-fold higher risk compared to the general population and a seven-fold increase in their first year on dialysis. These patients experience worse post-stroke outcomes due to factors like endothelial dysfunction and impaired cerebral autoregulation. Tailored stroke prevention strategies are necessary, as current

approaches mimic those for the general population. Intracranial imaging, underutilized in CKD/ESKD patients, could provide valuable insights for customizing dialysis regimens, particularly for high-risk individuals.

Materials and Methods. From May 2021 to May 2023, 39 ICH patients with CKD were identified out of 406 total ICH cases. Patients aged 42 to 76 years were included if they had spontaneous ICH in specific brain regions, excluding those with trauma, aneurysm rupture, or arteriovenous malformations. CKD causes included diabetic nephropathy (14 patients), hypertension (10 patients), both (11 patients), glomerulonephritis (2 patients), and IgA nephropathy (2 patients).

Results. The study included diverse CKD stages, with 20 patients in Stage 5. Notable correlations between severe renal dysfunction (eGFR <15 mL/min/1.73 m²) and worse clinical outcomes, particularly systolic blood pressure (SBP) on the third day post-ICH. Surgical interventions did not consistently lead to improved outcomes, emphasizing the importance of the patient's initial neurological condition.

Conclusion. Impaired renal function serves as an independent predictor of mortality and adverse outcomes in ICH patients. Hematoma volume, initial neurological status, and blood pressure control emerge as crucial prognostic factors. Meticulous management is essential, particularly for individuals with severe CKD, to mitigate complications and improve clinical outcomes.

Keywords: chronic kidney disease (CKD), intracerebral hemorrhage (ICH); prognostic factors, clinical outcomes, stroke risk

INTRODUCTION

Chronic kidney disease (CKD) represents a critical risk factor for stroke, encompassing both hemorrhagic and ischemic subtypes, with patients in end-stage kidney disease (ESKD) requiring renal replacement therapy facing a four-fold to ten-fold elevated risk in comparison to the general population, and a seven-fold risk increase during their initial year on dialysis.[1,2] Furthermore, CKD and ESKD patients tend to experience notably poorer functional outcomes and increased mortality after suffering a stroke.[3–5] The mechanisms underlying this heightened stroke risk in kidney disease patients involve various factors, including endothelial dysfunction, accelerated

arteriosclerosis, and impaired cerebral autoregulation.[6] Notably, there is an unmet need for stroke prevention measures tailored specifically to individuals with CKD, as current strategies resemble those employed in the general population without kidney disease.[7] Importantly, intracranial imaging is not a standard practice for CKD or ESKD patients; however, noninvasive imaging techniques may offer valuable insights for tailoring dialysis prescriptions or selecting dialysis modalities, especially for patients at elevated risk of stroke, where the optimization of dialysis options to mitigate systemic hypotension and cerebral hypoperfusion may be particularly beneficial.[8] Understanding these factors and implementing targeted prevention strategies is essential to mitigate the increased stroke risk in this patient population.

With this study, we aim to investigate and understand the determinants impacting the prognostic outcomes of 39 intracerebral hemorrhage (ICH) patients with coexisting chronic kidney disease (CKD). Our comprehensive analysis of these cases is intended to illuminate the complex interplay between CKD and ICH, thereby facilitating enhanced insights and the development of precise treatment strategies tailored to this high-risk patient population.

MATERIALS AND METHODS

Patient Population

During the period from May 2021 to May 2023, our institution admitted a total of 406 patients who had been diagnosed with intracerebral hemorrhage (ICH). Among this cohort, 39 patients, constituting 9.6% of the total, had a confirmed history of chronic kidney disease (CKD) and were selected for inclusion in this study. The age of these patients ranged from 42 to 76 years, with a mean age of 64 years. All 39 patients were specifically diagnosed with spontaneous ICH, and the location of the hemorrhage was determined in various brain regions, including the gangliocapsular region, thalamus, lobar areas, brainstem, and cerebellum, as confirmed by computed tomography (CT) scans.

Inclusion and Exclusion Criteria

In terms of inclusion criteria, this study encompassed patients who had received a diagnosis of spontaneous intracerebral hemorrhage (ICH) situated in specific brain regions. However, patients who had a documented history of trauma, aneurysm

rupture, or arteriovenous malformations were not considered for inclusion in the study and were subsequently excluded.

Causes and Severity of CKD

Within the cohort of 39 patients included in the study, chronic kidney disease (CKD) had various underlying causes, with the most prevalent being diabetic nephropathy in 14 patients, followed by hypertension in 10 patients, a combination of diabetic and hypertensive nephropathy in 11 patients, glomerulonephritis in 2 patients, and IgA nephropathy in 2 patients. The severity of CKD was assessed and categorized according to estimated glomerular filtration rate (eGFR) values.

Management of Patients

Following the diagnosis of intracerebral hemorrhage (ICH), immediate intravenous antihypertensive treatment with Labetolol was administered to maintain systolic blood pressure (SBP) below 160 mm Hg. Consultation with a nephrologist was sought for all patients, and those already undergoing maintenance hemodialysis continued their regimen. While the majority of patients were managed conservatively, surgical intervention was warranted in ten cases due to rapid neurological deterioration and midline shift. Surgical approaches involved open craniotomy for hematoma removal and the placement of an external ventricular drain.

Chronic kidney disease (CKD) stages were defined based on estimated glomerular filtration rate (eGFR) values, which indicate the kidney's filtering capacity in milliliters per minute per 1.73 square meters. Stage 1 corresponds to an eGFR equal to or greater than 90 mL/min/1.73 m², denoting relatively normal kidney function. Stage 2 encompasses eGFR levels between 60 and 89 mL/min/1.73 m², indicating mild kidney function reduction. As CKD progresses to Stage 3, eGFR falls within the range of 30 to 59 mL/min/1.73 m², representing moderate impairment. Stage 4, characterized by an eGFR of 15 to 29 mL/min/1.73 m², signifies severe kidney function decline. Finally, Stage 5 designates a critical phase with an eGFR below 15 mL/min/1.73 m², necessitating dialysis or kidney replacement therapy. These staged classifications offer a systematic framework for assessing the severity of kidney dysfunction, guiding the appropriate selection of medical interventions and treatments.

Imaging Analysis

CT scans were used to measure hematoma volumes on admission. Volumes were calculated assuming an ellipsoid shape [(π × width × depth × height)/6].

Analysis of Factors Affecting Clinical Outcomes

Clinical outcomes were assessed through the utilization of the modified Rankin Scale (mRS) during the final follow-up. A comprehensive analysis was conducted to examine the influence of various factors on these outcomes, including patient age, gender, length of hospital stay, initial hematoma volume, hematoma location, estimated glomerular filtration rate (eGFR), underlying medical conditions, prothrombin time, use of antiplatelet agents, presence of accompanying intraventricular hemorrhage (IVH), hemoglobin levels, diastolic blood pressure, and systolic blood pressure (SBP) both at the time of ICH onset and 3 days thereafter.

Ethical Considerations

This study was conducted following the guidelines of the Declaration of Helsinki. Ethical approval was obtained from the institutional review board, and informed consent was obtained from all patients involved in the study.

Statistical Analysis

Univariate analysis, including the Mann-Whitney U-test, chi-square test, independent 2-sample t-test, and logistic regression analysis, was conducted using SPSS ver. 20.0 (SPSS Inc., IBM) to explore relationships between variables and outcomes. Data were presented as mean ± standard deviation. Statistical significance was set at $p < 0.05$ for all analyses.

RESULTS

The study comprised 39 patients who had been diagnosed with intracerebral hemorrhage (ICH). These patients had a median age of 64 years, ranging from 42 to 76 years, with 28 males and 11 females among them. The median hematoma volume was 51.2 mL, with a range of 13.0 mL to 430 mL. Nine patients experienced concurrent intraventricular hemorrhage (IVH), and eight were using anti-platelet agents. The study sample displayed diversity in terms of chronic kidney disease (CKD) severity, with 20

patients in Stage 5, indicating critical kidney dysfunction. Hypertension (HTN) was the primary cause of CKD in 10 patients, followed by diabetes mellitus (DM) in 14 patients, and a combination of both in 11 patients. Regarding the location of ICH, gangliocapsular ICH was the most prevalent (n=15), followed by lobar (n=11), thalamus (n=5), brainstem (n=5), and cerebellum (n=3). The study population encountered various complications, including ICH-related mortality (n=7), sepsis-related mortality (n=3), cardiovascular complications (n=2), peripheral complications (n=3), rebleeding (n=10), and pulmonary embolism (n=1).

Neurological Status on Admission, Hematoma Volume, Renal Function, and Clinical Outcome

In this regression analysis aimed at assessing prognostic factors influencing neurological outcomes measured by the modified Rankin Scale (mRS), various key variables were taken into account. Notably, Glasgow Coma Scale (GCS) upon admission, hematoma volume, and estimated glomerular filtration rate (eGFR) exhibited substantial associations with clinical outcomes, evident from their low p-values ($p < 0.05$). A lower GCS score at admission demonstrated a robust correlation with less favorable neurological outcomes. Similarly, larger hematoma volumes and compromised renal function, as indicated by lower eGFR values, were linked to worse outcomes. On the contrary, factors such as age, hospital stay duration, blood pressure measurements, the presence of intraventricular hemorrhage (IVH), and the use of antiplatelet agents displayed no statistically significant connection with neurological status, as assessed by mRS. These findings underscore the significance of promptly evaluating neurological status upon admission, considering hematoma volume, and closely monitoring renal function as pivotal indicators in predicting clinical outcomes for individuals with intracerebral hemorrhage.

In the comparison of patients with severe renal dysfunction (eGFR <15 mL/min/1.73 m^2, Group A) and those with mild/moderate renal function (eGFR >15 mL/min/1.73 m^2, Group B), significant differences were observed in clinical outcomes. Group A, with lower renal function, exhibited higher systolic blood pressure (SBP) on the 3rd day and a higher incidence of rebleeding, resulting in a markedly worse neurological outcome (mean mRS score of 4.8±1.3) compared to Group B (mean mRS score of 3.2±1.5). The two groups did not significantly differ in initial Glasgow Coma Scale

scores, hematoma volumes, diastolic blood pressure, presence of intraventricular hemorrhage (IVH), or hemoglobin levels. These findings emphasize the critical impact of blood pressure control, particularly in patients with severe renal dysfunction, as uncontrolled hypertension led to rebleeding and significantly worse clinical outcomes in this subgroup.

The study investigated the relationship between hematoma volume, renal function, systolic blood pressure (SBP) on the 3rd day after intracerebral hemorrhage (ICH) development, and their connection to unfavorable outcomes, specifically mortality. The results revealed significant associations ($p < 0.05$) between an unfavorable outcome (mortality) and certain factors. Hematoma volume on admission, SBP on the 3rd day post-ICH, and modified glomerular filtration rate (eGFR) were found to be significantly related to mortality. Interestingly, the initial SBP did not demonstrate a significant association with unfavorable outcomes. These findings underscore the critical impact of these specific factors, emphasizing the importance of closely monitoring hematoma volume, renal function, and post-ICH SBP levels to predict and potentially mitigate unfavorable outcomes, particularly mortality, in patients with intracerebral hemorrhage.

The study aimed to investigate the influence of various factors on clinical outcomes among patients with both intracerebral hemorrhage (ICH) and chronic kidney disease (CKD). Regression analysis indicated that patient age, gender, length of hospitalization, hematoma location, concomitant intraventricular hemorrhage (IVH), and blood pressure at admission did not exert a significant impact on clinical outcomes (see Figure 2). The most frequently observed complications included rebleeding of the hemorrhage and peripheral issues such as deep vein thrombosis (DVT) and phlebitis. An inter-group analysis revealed no substantial relationship between CKD stage and the occurrence of complications. Nevertheless, a discernible trend suggested an inclination toward an increased incidence of complications in patients with more advanced renal dysfunction (Stage 4 and Stage 5 CKD). Specifically, cardiovascular complications like angina and myocardial infarction (MI) were noticed in patients with Stage 4 and Stage 5 CKD. Peripheral complications, such as DVT and phlebitis, were present in patients with Stage 3 and Stage 5 CKD. Rebleeding of the hemorrhage was more prominent in patients with Stage 5 CKD, while pulmonary embolism and sepsis were observed in patients at Stage 5 CKD. This analysis underscores a potential correlation between the severity of renal dysfunction and the occurrence of

complications in ICH patients with CKD, emphasizing the importance of vigilant monitoring and tailored management strategies, particularly for higher-stage CKD patients, to effectively mitigate these complications (refer to Table 3).

DISCUSSION

In this research, our primary objective was to elucidate the intricate relationship between chronic kidney disease (CKD) and clinical outcomes in patients suffering from intracerebral hemorrhage (ICH). The results of our investigation concur with the findings of previous studies,[7–11] which have consistently pointed to a grim prognosis for ICH patients with CKD, with reported mortality rates ranging from 43.8% to 83%. It is noteworthy, however, that our study revealed a relatively lower overall mortality rate of 25.6%. This discrepancy could potentially be attributed to the relatively smaller sample size in our study and the lower number of patients presenting with brainstem hemorrhages. Additionally, the reduced mortality rate in our study may be linked to the observation of smaller hematoma volumes, underscoring the potential impact of hematoma size on clinical outcomes.

Hematoma volume has garnered significant attention in the realm of intracerebral hemorrhage (ICH) research, with larger hematomas typically associated with more unfavorable outcomes. Previous studies[8,11] have underscored the connection between severe chronic kidney disease (CKD) and larger lobar hematomas. However, our regression analysis has brought forth a noteworthy finding, revealing that hematoma volume significantly impacts neurological outcomes, regardless of the various stages of renal dysfunction.

Renal function, assessed through glomerular filtration rate (GFR), has been a focal point in the evaluation of acute stroke patients. Our study substantiates the critical role of renal function in predicting outcomes, aligning with prior research findings.[5,11] It is apparent that patients with severe renal dysfunction (mGFR <15 mL/min/1.73 m²) experience markedly worse clinical outcomes. The intricacies of managing blood pressure in CKD patients, coupled with coagulation irregularities, elevate the risk of bleeding and vascular complications.[12] Notably, the control of systolic blood pressure on the third day post-ICH has emerged as a pivotal factor, underscoring the significance of continuous monitoring during the hospitalization period.

Furthermore, our investigation did not unveil significant correlations between clinical outcomes and factors such as age, gender, length of hospitalization, underlying renal disease, hematoma location, concurrent intraventricular hemorrhage, or the use of antiplatelet agents. While these findings may deviate from prior research, they accentuate the intricate interplay of multiple variables in shaping clinical outcomes.

With regard to interventions, our study offers insights into the nuanced domain of surgical management for ICH patients with CKD. The study underscores that surgical interventions do not invariably lead to improved outcomes, underscoring the paramount importance of the patient's baseline neurological condition.

The recognition of our study's limitations is essential, particularly in light of its retrospective design, the relatively small sample size, and the potential introduction of selection bias through the exclusion criteria. These constraints may impact the applicability of the study's findings to broader populations.

CONCLUSION

In summary, our study underscores the paramount significance of impaired renal function as a robust independent predictor of mortality and adverse outcomes in ICH patients. Hematoma volume, the patient's initial neurological status, and uncontrolled blood pressure emerge as crucial prognostic factors in this patient population. These findings underscore the imperative need for meticulous management, especially in individuals with severe chronic kidney dysfunction, to mitigate complications and enhance overall clinical outcomes. To further enhance our comprehension of the intricate interplay among these factors, it is imperative to conduct more extensive studies involving larger cohorts.

References

1. Coresh J, Astor BC, Greene T, Eknoyan G, Levey AS. Prevalence of chronic kidney disease and decreased kidney function in the adult US population: Third National Health and Nutrition Examination Survey. Am J Kidney Dis Off J Natl Kidney Found. 2003 Jan;41(1):1–12.
2. Nissenson AR, Pereira BJ, Collins AJ, Steinberg EP. Prevalence and characteristics of individuals with chronic kidney disease in a large health maintenance organization. Am J Kidney Dis Off J Natl Kidney Found. 2001 Jun;37(6):1177–83.
3. Briasoulis A, Bakris GL. Chronic kidney disease as a coronary artery disease risk equivalent. Curr Cardiol Rep. 2013 Mar;15(3):340.
4. Power A. Stroke in Dialysis and Chronic Kidney Disease. Blood Purif. 2013 Dec 20;36(3–4):179–83.
5. Krishna PR, Naresh S, Krishna GSR, Lakshmi AY, Vengamma B, Kumar VS. Stroke in chronic kidney disease. Indian J Nephrol. 2009 Jan;19(1):5–7.
6. Ghoshal S, Freedman BI. Mechanisms of Stroke in Patients with Chronic Kidney Disease. Am J Nephrol. 2019;50(4):229–39.
7. Kleindorfer D, Broderick J, Khoury J, Flaherty M, Woo D, Alwell K, et al. The unchanging incidence and case-fatality of stroke in the 1990s: a population-based study. Stroke. 2006 Oct;37(10):2473–8.
8. Murakami M, Hamasaki T, Kimura S, Maruyama D, Kakita K. Clinical features and management of intracranial hemorrhage in patients undergoing maintenance dialysis therapy. Neurol Med Chir (Tokyo). 2004 May;44(5):225–32; discussion 233.
9. Iseki K, Fukiyama K, Okawa Dialysis Study (OKIDS) Group. Clinical demographics and long-term prognosis after stroke in patients on chronic haemodialysis. The Okinawa Dialysis Study (OKIDS) Group. Nephrol Dial Transplant Off Publ Eur Dial Transpl Assoc - Eur Ren Assoc. 2000 Nov;15(11):1808–13.
10. Onoyama K, Kumagai H, Miishima T, Tsuruda H, Tomooka S, Motomura K, et al. Incidence of strokes and its prognosis in patients on maintenance hemodialysis.

Jpn Heart J. 1986 Sep;27(5):685–91.

11. Molshatzki N, Orion D, Tsabari R, Schwammenthal Y, Merzeliak O, Toashi M, et al. Chronic kidney disease in patients with acute intracerebral hemorrhage: association with large hematoma volume and poor outcome. Cerebrovasc Dis Basel Switz. 2011;31(3):271–7.
12. Beuscher VD, Sprügel MI, Gerner ST, Sembill JA, Madzar D, Reindl C, et al. Chronic Kidney Disease and Clinical Outcomes in Patients with Intracerebral Hemorrhage. J Stroke Cerebrovasc Dis Off J Natl Stroke Assoc. 2020 Aug;29(8):104802.